## REMARKS

The Office Action mailed March 26, 2006 has been carefully considered and the following response prepared. Claims 14-26, 29-37 and 40 are pending.

At page 2 of the Office Action, the Examiner rejected claims 14-26, 29-37 and 40 under 35 USC 112, first paragraph as not enabled because the specification does not reasonably provide enablement for any embodiment other than transformation with sequences disclosed in the specification.

Applicants' representative, Liza D. Hohenschutz, would like to thank Examiner Fronda for the helpful telephone interview on May 30, 2006 during which the instant rejection was discussed. Examiner Fronda advised Ms. Hohenschutz that showing genes from species other than *Corynebacterium* can be successfully expressed in *Corynebacterium* species would be helpful in overcoming the rejection.

Applicants traverse this rejection. Patent applicants must disclose their invention with sufficient detail so that persons skilled in the pertinent art can make and use the claimed invention without undue experimentation. *Chiron Corp. v. Genentech, Inc.*, 363 F.3d 1247 (Fed. Cir. 2004). Enablement of patent claims is determined by reference to the disclosures of the patent itself and the knowledge of persons skilled in the pertinent art at the time the patent application was filed.

At the time the present application was filed, nucleotide sequences encoding ilvD and ilvBNC from species other than *Corynebacterium glutamicum* were known in the art. Persons skilled in the art also had a reasonable expectation that nucleotide sequences from other organisms, including ilvD and ilvBNC sequences, could be transformed into *Corynebacterium* species and successfully expressed because transformation and expression of heterologous genes in *Corynebacterium* species had been accomplished with a variety of sequences. Undue experimentation is not required to make and use the claimed invention.

As discussed in Applicants' response filed January 19, 2006, at the priority date of the present application, the enzymes associated with biosynthesis of the branched chain amino acid valine were well-characterized. This pathway is described, for example, in DeRossi *et al.*, Gene 166: 127-132 (1995). The nucleotide and protein

sequences of dihydroxy acid dehydratase (ilvD) were known from sources including *Clostridium pasteurianum* (GenBank Acc. no. L06666), *Schizosaccharomyces pombe* (GenBank acc. no. D89254), *Lactococcus lactis* (GenBank acc. no U92974) and *E. coli* (GenBank acc. no. M10303). The nucleotide and protein sequences of acetohydroxy acid synthase (ilvBN) were known from sources including *Lactococcus lactis* (GenBank acc. no. U92974), *Methanococcus aeolicus* (GenBank acc. no. U35458), *Leuconostoc mesenteroides* (GenBank acc. no. U50749), *Mycobacterium avium* (GenBank acc. no. L49392), *Streptomyces avermitilis* (GenBank acc. no. L39268), *Corynebacterium glutamicum* (GenBank acc. no. L09232) and *Bacillus subtilis* (GenBank acc. no. L03181). Isomeroreductase (ilvC) was known from sources including *Mycobacterium avium* (GenBank acc. no. L49392), *Streptomyces avermitilis* (GenBank acc. no. L39268), *Bacillus subtilis* (GenBank acc. no. L03818), *Corynebacterium glutamicum* (GenBank acc. no. L09232) and *Leuconostoc mesenteroides* (GenBank acc. no. U50749). Thus, only routine experimentation would be required to obtain polynucleotide sequences encoding ilvD and ilvBNC from other species.

*Corynebacterium* species, such as *Corynebacterium glutamicum* and related species such a *Brevibacterium flavum* and *Brevibacterium lactofermentum* are well-known industrially important bacteria that are widely used for the fermentative production of amino acids. Before the priority date of the present application, it was well-known in the art to use *Corynebacterium* species for expression of heterologous proteins. Billman-Jacob *et al.*, Applied and Environmental Microbiology 61: 1610-1613, 1995, a copy of which is attached, discusses *C. glutamicum* and its use for producing large quantities of amino acids on an industrial scale at page 1610, left column. The authors state that the genetics of amino acid synthesis by *C. glutamicum* has been studied extensively, and that the application of recombinant DNA techniques to *C. glutamicum* has given the bacterium the ability to use foreign genes and product recombinant proteins. The authors listed five foreign genes that had been successfully expressed by *C. glutamicum,* including bacterial genes involved in amino acid synthesis (referring to a publication on the threonine operon of *E. coli*). In the paper, the authors cloned and expressed the basic protease gene of *Dichelobacter nodosus* and the subtilisin gene of *Bacillus subtilis* in *C. glutamicum*. In another report, Menkel *et al.*, Applied and

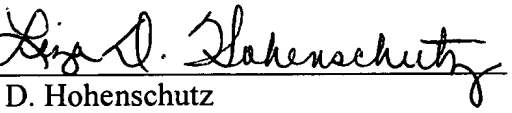
Environmental Microbiology 55: 684-688, 1989, discloses transformation and expression of the *E. coli* aspartase ($aspA^+$) gene in *C. glutamicum*. In strains expressing the *E. coli* aspartase, the authors found increased excretion of lysine.

In summary, the specification enables persons skilled in the pertinent art to make and use the claimed invention without undue experimentation. At the time the present application was filed, persons skilled in the art had a reasonable expectation that polynucleotide sequences encoding ilvD and ilvBNC from sources other than *C. glutamicum* could be expressed in *Corynebacterium* species because expression of a variety of heterologous genes in *Corynebacterium* was known in the art. Moreover, ilvD and ilvBNC genes from other sources were known, and only routine experimentation would be required to obtain and use such sequences. Withdrawal of this section 112, first paragraph rejection is requested.

In view of the above, the present application is believed to be in a condition ready for allowance. Reconsideration of the application is requested and an early Notice of Allowance is earnestly solicited.

Dated: July 26, 2006

Respectfully submitted,

By 

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